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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Multivalent Immunogenic Peptides (Vaccines) for the Treatment of Prostate and Breast Cancer

Description of Technology: The development of more targeted means of treating cancer is vital. One option for a targeted treatment is the creation of a vaccine that induces an immune response only against cancer cells. In this sense, vaccination involves the introduction of a peptide into a patient that causes the formation of antibodies or T cells that recognize the peptide. If the peptide is from a protein found selectively on/in cancer cells, those antibodies or T cells can trigger the death of those cancer cells without harming non-cancer cells. This can result in fewer side effects for the patient.

TARP (T cell receptor gamma alternate reading frame protein) is a protein that is selectively expressed on the cells of about 95% of prostate cancers and about 50% of breast cancers. This invention concerns the identification of a combination of immunogenic peptides within TARP and their use to create an anti-cancer immune response in patients. By introducing these seven peptides into a patient, an immune response against these cancer cells can be initiated by the peptides, resulting in treatment of the cancer.

Potential Commercial Applications:

- Peptides can be used as vaccines to induce an immune response against cancer
- Treatment of any cancer associated with increased or preferential expression of TARP
- Specific diseases include breast cancer and prostate cancer

Competitive Advantages:

- Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients
- Use of multiple peptides permits production of a more thorough complement of T cells against the antigen

Development Stage:

- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)

Inventors: Jay A. Berzofsky, et al. (NCI)

Publications:

1. Epel M, et al. Targeting TARP, a novel breast and prostate tumor-associated antigen, with T cell receptor-like human recombinant antibodies. Eur J Immunol. 2008 Jun;38(6):1706-20. [PMID 18446790]
2. Oh S, et al. Human CTLs to wild-type and enhanced epitopes of a novel prostate and breast tumor-associated protein, TARP, lyse human breast cancer cells. Cancer Res. 2004 Apr 1;64(7):2610-8. [PMID 15059918]

Intellectual Property: HHS Reference No. E-047-2014/0 – US Provisional Patent Application No. 61/915,948 filed 13 Dec 2013

Related Technologies: HHS Reference No. E-116-2003/0 –

- US Patent No. 8,043,623 issued 02 Jun 2009
- US Patent No. 7,541,035 issued 25 Oct 2011

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632;

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Collaborative Research Opportunity: The Vaccine Branch, CCR, NCI, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize cancer vaccines to induce T cell immunity against TARP to treat prostate and/or breast cancer. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Novel Immunocytokine for the Treatment of Cancer

Description of Technology: Mesothelin is a protein that is aberrantly expressed by several cancers, most notably malignant mesothelioma. Immunoconjugates that target mesothelin are currently being evaluated in clinical trials. Unfortunately, these immunoconjugates often use bacterial toxins as the payload, leading to the formation of neutralizing antibodies by patients and resulting in a reduction in therapeutic effectiveness over multiple administrations.

Interleukin-12 (IL12) is a protein that has potent anti-tumor, anti-angiogenic, and anti-metastatic properties. Although initially considered an attractive candidate as a cancer therapeutic, systemic administration of IL12 is toxic.

Inventors at the NIH have created an immunoconjugate using an anti-mesothelin antibody (SS1) as the targeting moiety and IL12 as the payload molecule. This allows the localized concentration of IL12 at cancer cells, reducing the toxic effects seen with systemic IL12 administration. Furthermore, using IL12 instead of a bacterial toxin helps to reduce the formation of neutralizing antibodies. The IL12-SS1 immunoconjugate is

able to inhibit the growth human malignant mesothelioma in mouse xenograft models, suggesting it has significant potential as a cancer therapeutic.

Potential Commercial Applications:

- Selective killing of cells that express mesothelin, such as those seen with particular cancers.
- Specific cancers include malignant mesothelioma, pancreatic cancer and ovarian cancer.

Competitive Advantages:

- Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients.
- Use of human IL12 as the payload may reduce formation of neutralizing antibodies against the molecule, increasing therapeutic effectiveness.

Development Stage:

- In vitro data available
- In vivo data available (animal)

Inventors: Mitchell Ho, et al. (NCI)

Publication: Kim H, et al. Novel immunocytokine IL12-SS1(Fv) inhibits mesothelioma tumor growth in nude mice. PLoS One. 2013 Nov 15;8(11):e81919. [PMID 24260587]

Intellectual Property: HHS Reference No. E-118-2013/0 – US Provisional Patent Application 61/820,523 filed 07 May 2013

Related Technology: HHS Reference No. E-139-1999/0 – U.S. Patent 7,081,518 issued 25 July 2006

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632;

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Collaborative Research Opportunity: The NCI Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize the immunocytokine-based therapy targeting mesothelin-expressing tumors. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Improved Personalized Cancer Immunotherapy: Rapid Selection of Tumor Reactive T Cells Based on Expression of Specific Cell Surface Markers from Peripheral Blood

Description of Technology: Scientists at NIH have identified a process to select highly tumor-reactive T cells from a patient's peripheral blood sample based on the expression of two specific T cell surface markers: programmed cell death protein 1 (PD-1; CD279) and/or T cell Ig- and mucin-domain-containing molecule-3 (TIM-3). After this enriched population of tumor-reactive T cells is selected and expanded to large quantities, it gets re-infused into the patient via an adoptive cell transfer (ACT) regimen. The key finding for this process is that the most tumor-reactive T cells found in a bulk population of cells obtained from a patient's peripheral blood sample reliably exhibit high expression of at least one of these markers. The enrichment of tumor-reactive cells from a patient's peripheral blood based on these markers provides a simple alternative to the current strategies based on isolation tumor-reactive cells from the tumor, as it reduces the cost

and complications of tumor resection, as well as provides a T cell product for patients without resectable lesions.

This new method for selecting tumor-reactive T cells from peripheral blood samples should help ACT immunotherapy become more GMP compliant and allow greater standardized of the production process to enable more widespread utilization of this personalized cancer treatment approach outside of NIH.

Potential Commercial Applications:

- Personalized ACT immunotherapy to treat cancers using T cells obtained from a peripheral blood.
- Possible integration into a standard procedure for obtaining tumor-reactive T cells from a peripheral blood as part of a GMP-compliant manufacturing process that gains regulatory approval as a personalized cancer treatment option.
- The immunotherapy component of a combination cancer therapy regimen targeting specific tumor antigens in individual patients.
- More rapid tumor-reactive T cell culturing process for laboratory testing.

Competitive Advantages:

- Simpler: Tumor-reactive T cells can be selected for ACT from a bulk population derived from peripheral blood sample using common laboratory techniques.
- More rapid: Selection of T cells based on expression of specific cell surface markers will reduce the culture time for these T cells before reinfusion into the patient to fight the tumor.
- Less screening: This selection method eliminates the need to screen T cells for autologous tumor recognition before re-infusion into the patient.

Development Stage:

- Early-stage
- In vitro data available

Inventors: Alena Gros and Steven A. Rosenberg (NCI)

Intellectual Property: HHS Reference No. E-085-2013/0 –

- US Provisional Application No. 61/771,251 filed 01 March 2013
- PCT Application No. PCT/US2013/38813 filed 30 April 2013

Related Technologies: HHS Reference No. E-059-2013 –

- US Provisional Application No. 61/771,247 filed 01 March 2013
- PCT Application No. PCT/US2013/038799 filed 30 April 2013

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